REMARKS/ARGUMENTS

This is in response to the Office Action mailed May 12, 2005 for the above-captioned application. Reconsideration and further examination are respectfully requested.

The specification has been corrected in view of the Examiner's remarks. Applicants respectfully request, however, that in the future the Examiner refer to paragraph numbers rather than page numbers in electronically filed applications, since the page on which materials occur in these applications can be very different depending on the location at which they are printed.

Claims 14-17, 25 and 26 stand rejected under 35 USC § 112, first paragraph, for failure to comply wit the written description requirement. Applicants have amended claim 14 to refer to a specific target sequence, which is Seq. ID No. 91 which was present in the application as filed. Given the Examiner's remarks, it is believed that this amendment overcomes the rejection.

The Examiner rejected claims 14-17, 19 and 25-28 as anticipated by Baracchini (US 5,801,154). Baracchini does not disclose any oligonucleotide that is complementary to Seq ID. No. 91. Furthermore, there is no oligonucleotide in Baracchini that has a "consecutive series of bases" that is the same as in Seq. ID No. 82. The Examiner's first example of an oligonucleotide is Seq ID No. 6 in Baracchini. This sequence when compared to Seq. ID No. 82 clearly has no similarity.

TCGGAGCCAT CGGCGCTGCA

GGGACGCGGC GCTCGGTCAT

The Examiner supports the strange argument that Baracchini Seq. 6 anticipates Seq. ID 82 of this application by saying that the term "'comprising a consecutive series of basis' is being interpreted as referring to comprising any consecutive series of bases in any portion of Seq. ID No. 82. How this interpretation of the claim makes any sense in the context of the invention, or in the context of claim 19 being dependent and requiring activity relative to hsp27 is unclear. The plain meaning of "consecutive" is "following one another in uninterrupted succession or order; successive." The Examiner has failed to give this, or any other reasonable meaning to the word "consecutive" however.

For these reasons, the rejection based on Baracchini should be withdrawn.

The Examiner also rejected claims 14, 15, 25 and 26 as anticipated by Brophy (US 2003/0060399). Without conceding that Brophy is prior art, Applicants note that Brophy does not disclose an antisense complementary to Seq. ID No. 91. The Examiner's arguments in the §

112 rejection concerning other sequences for hsp27 make it clear that the mere mention of antisense targeting hsp27 does not teach or imply any specific structures. Accordingly, Brophy is not anticipatory and the rejection should be withdrawn.

The Examiner also rejected claims 14 and 15 as anticipated by Hargis et al. This abstract discloses research but not pharmaceutical applications for hsp27 antisense. No sequences or source of the oligonucleotides are disclosed. Thus, the reference fails to anticipate the claimed invention because it discloses neither the sequences as claims nor any reason to make a therapeutic composition.

Finally, the Examiner rejected claims 14-17, 19, and 25-28 as obvious over Horman in view of Taylor, Baracchini and Bennett. As a first matter, Applicants point out that no reference identifiable as "Taylor" was provided with the Office Action or listed on a 1449 or 892 form in this case. Accordingly, if the rejection is maintained, it should be in a non-final action in which the reference is fully identified and provided. From the Examiner's remarks, however, it appears that "Taylor" is not specific to hsp27 and is, like Baracchini and Bennett, only related to antisense technology generally. On this assumption, Applicants will respond to the rejection.

The Examiner asserts that Horman et al teach antisense inhibition of hsp27 expression in MCF-7 mammary carcinoma cells, and that the antisense cDNA utilized by Horman would inherently comprise a consecutive series of bases as set forth in Seq. ID No. 82. Horman is also said to teach that hsp27 is overexpressed in pre-malignant and malignant lesions in rat and human liver.

Taylor is cited for a teaching that "antisense oligonucleotides 7-30 nucleotides long can be synthesized to inhibit the expression of any protein provided the cDNA sequence is known." Taylor and Baracchini and Bennett are all cited for general teachings of backbone modifications. As a result of these generalized disclosures is an assertion by the Examiner that one would have been motivated to antisense oligonucleotide targeted to hsp27 and place it in a pharmaceutical composition. Applicants respectfully disagree.

First of all, in order for it to be obvious to place something in a pharmaceutical composition, or to use it in therapy, there must be knowledge in the art of therapeutic utility. That knowledge is not present here. The Examiner relies solely on a teaching that hsp27 is overexpressed in pre-malignant or malignant lesions. However, the Horman reference provides no basis to know whether this overexpression is a cause of the development of malignancy, a consequence of the development of malignancy, or perhaps even unrelated. Indeed, the Horman reference contains a bare mention of these observations as something that was reported in the early 1990's and does not develop it further into any suggestion of a therapeutic.

Furthermore, looking at the question actually addressed by the Horman paper, as opposed to its statement of that which came before, the paper investigated whether HSP27 "might play a regulatory function in proliferation and differentiation." (Page 577, Col. 1) It found that while reduction in hsp27 levels reduced growth rate, it did not increase the rate of cell death. (Page 578, Col. 2). The paper also reports that in other studies transfection with hsp27, and the resulting high levels of hsp27 resulted in cellular inhibition. (Id.) Indeed, they conclude that "we do not suggest that HSP27 necessarily plays a role in specifying cell behavior, but that, when it intervenes, it would by being permissive or not of a programme which is determined otherwise by the genetic potential and the status of the cell." (Page 580, Col. 1) Nothing in the Horman paper clearly suggests that regulation of hsp27 expression directly has potential for therapeutic efficacy, and thus nothing suggests placing anti-hsp27 antisense in a therapeutic preparation.

Applicants further note that Horman utilizes full length anti-hsp27 antisense of which copies are made *in vivo*, not a preparation containing the antisense or an anti-hsp27 antisense oligonucleotide. The Examiner's generalized teachings about making antisense oligonucleotides are not sufficient to render claims to anti-hsp27 antisense oligonucleotides and the use of such oligonucleotides obvious. Furthermore, the Examiner's statement of the content of the Taylor paper is inconsistent with the knowledge in the art. Merely knowing the sequence of a cDNA does not render antisense oligonucleotides obvious, because not all possible oligonucleotide sequences are effective as antisense. Furthermore, nearly knowing the sequence does not render any particular antisense oligonucleotide, such as Seq. ID No. 82 obvious, absence some evidence or reasoning that selection of this particular sequence is guided by the art.

For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Applicants enclose a supplemental Information Disclosure Statement, together with copies of the non-patent references and the fee for filing of a disclosure statement after the first action on the merits. Acknowledgment of the filing and consideration of the listed references are requested.

Respectfully submitted,

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